REMARKS/ARGUMENTS

In response to the Office Action of August 7, 2003, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

No new matter has been added by the amendments to the specification.

A protocol in the experimental section of the detailed description has been amended to properly identify the trademark SEPHAROSE using capitalization.

The abstract has been amended to remove the legal phraseology ("said").

Claim 1 has been amended. Claims 2-35 were previously canceled. Claims 36-43 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1 and 36-43 are pending in the instant application.

No new matter has been added by the amendment to claim 1. The amendment is made to clarify that the claimed biopolymer marker peptide is isolated from its natural state (see page 29, line 9 and page 31, lines 9-12 of the instant specification).

Request for Rejoining of Claims

Applicants respectfully submit that the Examiner has misinterpreted the request for rejoining of claims under *Ochiai* in the Response filed in May 30, 2003. The request for rejoining was

intended for consideration **after** the claims of Group I reading on the biopolymer marker peptide are found allowable. The request for rejoining was not intended to be a traversal of the restriction requirement. The request for rejoining is reiterated below for the convenience of the Examiner.

The instant application is related in claim format to several pending applications of which serial number 09/846,352 is exemplary. The biopolymer marker of serial number 09/846,352 was found to be novel and subsequently claims reading on methods and kits limited to its use were rejoined with the claims reading on the biopolymer marker under *Ochiai*. Similarly, if the peptide consisting of amino acid residues 2-11 of SEQ ID NO:1 of the instant application is found to be novel, methods and kits limited to its use should also be novel. Thus, in an effort to maintain equivalent scope in all of these applications, Applicants respectfully request that the Examiner enter the new claims (36-43) added previously by amendment and consider rejoining them with the claim (claim 1) reading on the biopolymer marker peptide consisting of amino acid residues 2-11 of SEQ ID NO:1 after such claim to the biopolymer marker peptide is found allowable.

Sequence compliance

On pages 10 and 11 of the Response filed on May 30, 2003, Applicants indicated that amino acid residues 1 and 12 of SEQ ID

NO:1 were necessary for protein purification. A more complete explanation of the inclusion of amino acid residues 1 (H) and 12 (R)to SEQ ID NO:1 is presented herein.

The first (H) and last (R) amino acid residues of SEQ ID NO:1 are shown in parentheses in the figures. When carrying out mass spectrometric procedures, it is possible to fragment a whole molecule, depending upon the enzyme used for digestion. A sequence is often predicted from these fragments but often the sequence is not identified completely. It is conventional in the art to show the missing portions of the predicted sequence in parentheses. The first and last amino acid residues of SEQ ID NO:1 are predicted residues as disclosed by the parentheses in the figures. SEQ ID NO:1 without the first and last predicted amino acid residues was shown on page 27, line 18 of the original disclosure. Thus, no new matter has been added in the filing of the substitute Sequence Listing on May 30, 2003. The first and last amino acid residues of SEQ ID NO:1 are disclosed in the figures and the Sequence Listing, however the biopolymer marker peptide identified in patient sera consists of amino acid residues 2-11 of SEQ ID NO:1. The amendments made previously to the claims and specification limiting the marker sequences to specific amino acid residues are made for the purpose of clarification of the use of parentheses only. The claims as previously amended limit the biopolymer marker peptide sequence to amino acid residues 2-11 of SEQ ID NO:1.

Objection to the Drawings

The Examiner alleges that the transmittal letter submitting formal drawings filed on May 30, 2003 was accompanied by four formal drawings. The fourth formal drawing stands objected to by the Examiner for containing numbers that are written upside down and backwards.

Applicants respectfully submit that the Examiner has confused the formal drawings with the single drawing attached to the Declaration Under 37 CFR 1.132 also filed on May 30, 2003. There were three formal drawings submitted with the transmittal letter of May 30, 2003 labeled Figure 1, Figure 2A and Figure 2B. There was one figure showing two spectra labeled MI and NHS submitted with the Declaration on May 30, 2003. A copy of this figure (as intended to accompany the declaration) containing corrected numbering is filed herewith. A copy of the text of the Declaration filed on May 30, 2003 is filed herewith for the convenience of the Examiner.

Thus, Applicants respectfully submit that they have clarified the Examiner's objection to the drawings and request that this objection now be withdrawn.

Rejection under 35 USC 101

Claim 1, as originally presented, stands rejected under 35 USC 101 because the claimed invention allegedly lacks patentable

utility due to its not being supported by a specific, substantial and credible utility, or in the alternative, a well-established utility.

The Examiner alleges that the claimed polynucleotide is not supported by a substantial utility, because no substantial utility has been adequately established for the claimed subject matter. The Examiner further alleges that no mention is made in the instant specification of control samples in comparison to the actual claimed biomarker from disease states and that further research is required to confirm a "real world" context of use.

Applicants respectfully disagree with the Examiner's assertions. Claim 1 has been amended herein to recite an isolated biopolymer marker peptide. This amendment is made to clarify that the biopolymer marker has been isolated by "the hand of man" from its natural state (supported at page 29, line 9 and page 31, lines 9-12 of the instant specification).

Claim 1 is limited to a specific biopolymer marker peptide (amino acid residues 2-11 of SEQ ID NO:1) with a specific utility (diagnostic for myocardial infarction, congestive heart failure and intracerebral hemorrhage). By this claim, Applicants have asserted that the claimed invention has a particular practical purpose; which by itself should satisfy the utility requirements (see MPEP 2107, II(B)(1)).

The instant inventors do not attempt to develop a reference

"normal", but rather strive to specify particular markers which are evidentiary of at least one specific disease state, whereby the presence of said marker serves as a positive indicator of disease (see page 5, lines 7-11 of the instant specification). Applicants claim that the presence of amino acid residues 2-11 of SEQ ID NO:1 is a positive indicator of myocardial infarction, congestive heart failure and intracerebral hemorrhage. This is a specific, substantial and a credible utility that was established at the time of filing by the data shown in Figure 1. Figure 1 displays a table listing patients having a history of myocardial infarction, intracerebral hemorrhage and congestive heart failure. All of the patients listed show the presence of amino acid residues 2-11 of SEQ ID NO:1 in their serum.

The Examiner alleges that no mention has been made of control samples, however, Applicants respectfully disagree with the Examiner's assertions. A Declaration Under 37 CFR 1.132 with an attached figure was filed with the Response to the Restriction Requirement (filed on May 30, 2003). The bottom of page 11 (of the Response to the Restriction Requirement) under the heading "Declaration Under 37 CFR 1.132, states "A declaration under 37 CFR 1.132 is filed concurrently herewith in order to provide evidence of the absence of the biopolymer marker peptide (amino acid residues 2-11 of SEQ ID NO:1) weighing 1211 daltons in normal human serum." This declaration with attached figure establishes control

samples.

A copy of the Declaration Under 37 CFR 1.132 (with an attached figure containing corrected numbers) is filed herewith for the convenience of the Examiner. In order to further evidence that the claimed biopolymer marker peptide (amino acid residues 2-11 of SEQ ID NO:1; the 1211 dalton marker) can be used to identify patients having a history of myocardial infarction, Applicants herein provide the attached Declaration (and Figure) under 37 CFR 1.132. The profiles shown in the figure attached to the declaration indicate that the claimed biopolymer marker peptide can be used to distinguish individuals suffering from myocardial infarction from those not inflicted with myocardial infarction. The figure attached to the declaration provides side-by-side profiles (obtained using techniques of mass spectrometry) of normal human sera (bottom panel)versus sera from patients having a history of myocardial infarction (top panel). This profile comparison clearly evidences the absence of the 1211 dalton marker in normal human sera and thus establishes the specificity of the 1211 dalton peptide as a marker which when present in the sera is diagnostic for myocardial infarction. The spectra in the figure were obtained from the data gathered in the original experiments and thus do not represent "new" or additional experimentation conducted after the time of the invention.

Thus, Applicants have provided a specific, substantial and a

credible utility (diagnostic for myocardial infarction, congestive heart failure and intracerebral hemorrhage) for the claimed biopolymer marker peptide (amino acid residues 2-11 of SEQ ID NO:1). Furthermore, Applicants have provided control samples evidencing this utility.

As evidenced by the above discussion, Applicants have clarified the specific, substantial and credible utility of the claimed invention and respectfully request that this rejection now be withdrawn.

Rejection under 35 USC 112, first paragraph

Claim 1, as originally presented, stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which with it is most nearly connected, to make and/or use the invention.

The Examiner alleges that one of ordinary skill in the art would not know how to use any asserted specific or substantial utility of the claimed biopolymer marker when the patient samples have not been appropriately compared to controls from which to draw valid conclusions of use. The Examiner further alleges that since the claimed invention is not supported by a specific, substantial and credible utility or a well-established utility for the reasons set forth in the 35 USC 101 rejection, one skilled in the art would

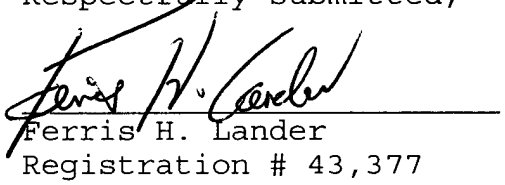
not know how to use the claimed invention.

Applicants respectfully disagree with the Examiner's assertions. As clarified in the above discussion (Rejection Under 35 USC 101), the claimed invention is supported by a specific, substantial and credible utility (a well-established utility). Claim 1 is limited to a specific biopolymer marker peptide (amino acid residues 2-11 of SEQ ID NO:1) specifically diagnostic for myocardial infarction, congestive heart failure and intracerebral hemorrhage. The presence of amino acid residues 2-11 of SEQ ID NO:1 is a positive indicator of myocardial infarction, congestive heart failure and intracerebral hemorrhage as shown by the data presented in Figure 1. In light of this specific, substantial and credible utility, Applicants assert that one of ordinary skill in the art when reviewing the instant specification would recognize how to use the claimed sequence (amino acid residues 2-11 of SEQ ID NO:1) as a marker for myocardial infarction, congestive heart failure and intracerebral hemorrhage. Thus, Applicants respectfully request that this rejection now be withdrawn.

CONCLUSION

In light of the foregoing remarks, amendments to the specification and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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